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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,373	09/28/2001	Patrick J. Muraca	5568/1042	3910

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,373	MURACA, PATRICK J.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2004 and 15 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *17-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 4/15/04 and 5/13/04, are acknowledged. Amended claims 1, 3, and 4 are acknowledged.

Applicant's arguments, filed 4/15/04 and 5/13/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-16 are herein under examination.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by amendment.

Applicants did not point to any support within the specification, drawings, or claims, as originally filed for the newly amended phrase "wherein each sample of the microarray exhibits a biological characteristic representative of a stage of cancer" as newly stated in amended claims

1, 3, and 4. The abstract states the phrase "each sample represents a different stage of cancer"; however, this does not provide support for *each* sample *exhibiting a biological characteristic representative* of a stage of cancer, which differs in scope. No mention is made as to whether such representative biological characteristics are exhibited in each sample. Because the introduction of "wherein each sample of the microarray exhibits a biological characteristic representative of a stage of cancer" lacks proper written support in amended claims 1, 3, and 4, filed 5/13/04, this phrase is considered NEW MATTER. Claims 2 and 5-16 are also rejected due to their direct or indirect dependency from claims 1, 3, and 4. This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

Claims 1, 3, and 4 recite the phrase "exhibits a biological characteristic representative of a stage of cancer" which is vague and indefinite. It is unclear what criteria and to what degree these criteria must be met for the exhibited biological characteristic to be considered "representative of a stage of cancer." Clarification of the metes and bounds of this phrase via clearer claim wording is requested. Claims 2 and 5-16 are also rejected due to their direct or indirect dependency from claims 1, 3, and 4.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1, 2, 5, 6, 10-13, and 15-16 is maintained under 35 U.S.C. 102(e)(2) as being anticipated by Lincoln et al. (P/N 6,553,317).

This rejection is maintained and reiterated for reasons of record. The amended phrase "wherein each sample of the microarray exhibits a biological characteristic representative of a stage of cancer" in claim 1 is not addressed as it is considered NEW MATTER that must be deleted.

Lincoln et al. disclose the use of bioinformatics to study genes differentially expressed or commonly expressed in different tissues or cell lines, such as normal (normally proliferating cells) and cancerous tissue (abnormally proliferating cells) (col. 1, lines 46-48). Lincoln et al. disclose using a microarray with multiple samples (col. 3, lines 10-12). Lincoln et al. disclose processing clones in groups on a 96-well plastic culture dish with each chamber/well comprising an indentation in the dish to separate samples (col. 12, lines 20-25) which represents a stably associated samples with a distinct, known sublocation on a substrate, as stated in instant claim 1. Lincoln et al. disclose a barcode (identifier) for a lot or 96-well plate whose value is placed in a

barcode field of a table in a database (col. 21, lines 30-41) which represents a substrate with an identifier that provides access to a database, as stated in instant claim 1. The samples in a plastic culture dish represent the sample (tissue or cells) being plastic-embedded, as stated in instant claim 10. The information on the plastic culture dish, including precise sample location with lot and well information, is recorded for each sample and given to customers (col. 12, lines 29-36). Lincoln et al. disclose using a relational database system for storing biomolecular sequence information with biological annotations (col. 2, lines 14-20) including information identifying (identifiers) sequences (col. 2, lines 28-34). Lincoln et al. disclose a system allowing a user to selectively view information regarding sequences and reagent specifications (col. 2, lines 34-37) including a graphical user interface where a query is entered and matches between query and information is displayed (col. 2, lines 46-50). Lincoln et al. disclose using a relational database with tables (col. 15, lines 44-49) including a library table that includes records of each library in the gene expression database including an identifier (LibraryID) (col. 16, lines 7-9). Lincoln et al. disclose the library table as having a "TissueID" attribute that is inherited from a "TissueSpecimen" table) and a "Tissue_Category" attribute as well as a "Lib_Description" attribute including information such as tissue name, disease state, patient age/gender (col. 16, lines 6-32). Lincoln et al. disclose providing further information about a donor in a "MedicalHistory" table including information such as a problem such as breast cancer, breast, and neoplasm (col. 20, lines 33-40), as stated in instant claim 6. Lincoln et al. disclose using a network to which the network server and clients are connected (col. 13, lines 3-9). Lincoln et al. disclose entries in various results screens may provide links to other information in the database (col. 23, lines 10-13) as stated in instant claim 2. Lincoln et al. disclose each tissue specimen (as

uniquely identified by TissueID) may have several diagnoses (i.e. normal, diseased, involved, cancerous) and each donor may provide multiple tissue specimens (col. 19, lines 35-67). This act of providing multiple tissue specimens that are "cancerous" or "involved" is reasonably interpreted to include specimens from sites of a secondary metastasis of cancer, as stated in instant claim 16. Lincoln et al. disclose different development stages (col. 20, lines 13-14) as stated in claim 11. Lincoln et al. disclose studying or monitoring drug resistance in certain tissue (col. 5, lines 1-3) which represents substantially homogeneous cells (as stated in instant claim 13) and samples from patients treated with a drug (as stated in instant claim 15).

Thus, Lincoln et al. anticipate the limitations in claims 1, 2, 5, 6, 10-13, and 15-16.

Applicants state their amended phrase including the limitation of "wherein each sample of the microarray exhibits a biological characteristic representative of a stage of cancer" is part of the claimed invention. This is confusing as instant claim 5 comprises normally proliferating cells which suggests normal cells that are not representative of a cancerous stage. Applicants state the claimed invention allows for the comparison of a patient's tissue and/or cell sample with the samples of the microarray to determine the progression of the patient's illness. While this statement may be true, such determination of illness progression is considered irrelevant in comparison to prior art as this determination is not disclosed in the instant claims. Applicants state that Lincoln et al. do not disclose a microarray and then state that Lincoln et al. disclose "microarray" in two passages. Lincoln et al. clearly disclose a microarray, as stated in column 3 (line 12), column 8 (line 67), and column 9 (lines 3-4). Applicants state that Lincoln et al. recitation of a microarray does not anticipate an oncology microarray wherein each sample

exhibits a biological characteristic representative of a stage of cancer. This is found unpersuasive as such a microarray with each sample exhibiting a biological characteristic representative of a stage of cancer appears to be NEW MATTER and not specifically mentioned in the instant application. Lincoln et al. clearly disclose the study of cancerous tissue and the use of a microarray, as disclosed above.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-16 is maintained under 35 U.S.C. 103(a) as being unpatentable over Lincoln et al. (P/N 6,553,317) in view of Schraml et al. (Clinical Cancer Research, August 1999, vol. 5, pages 1966-1975) and Lehman et al. (Cancer Research, February 2000, vol. 60, pages 1062-1069).

This rejection is maintained and reiterated for reasons of record. The amended phrase "wherein each sample of the microarray exhibits a biological characteristic representative of a stage of cancer" in claims 1, 3, and 4 is not addressed as it is considered NEW MATTER that must be deleted.

Lincoln et al. describe the use of bioinformatics to study genes differentially expressed or commonly expressed in different tissues or cell lines, such as normal (normally proliferating cells) and cancerous tissue (abnormally proliferating cells) (col. 1, lines 46-48). Lincoln et al. describe using a microarray with multiple samples (col. 3, lines 10-12). Lincoln et al. describe processing clones in groups on a 96-well plastic culture dish with each chamber/well comprising an indentation in the dish to separate samples (col. 12, lines 20-25) which represents a stably associated samples with a distinct, known sublocation on a substrate, as stated in instant claim 1. Lincoln et al. describe a barcode (identifier) for a lot or 96-well plate whose value is placed in a barcode field of a table in a database (col. 21, lines 30-41) which represents a substrate with an identifier that provides access to a database, as stated in instant claim 1. The samples in a plastic culture dish represent the sample (tissue or cells) being plastic-embedded, as stated in instant claim 10. The information on the plastic culture dish, including precise sample location with lot and well information, is recorded for each sample and given to customers (col. 12, lines 29-36). Lincoln et al. describe using a relational database system for storing biomolecular sequence information with biological annotations (col. 2, lines 14-20) including information identifying (identifiers) sequences (col. 2, lines 28-34). Lincoln et al. describe a system allowing a user to selectively view information regarding sequences and reagent specifications (col. 2, lines 34-37) including a graphical user interface where a query is entered and matches between query and information is displayed (col. 2, lines 46-50). Lincoln et al. describe using a relational database with tables (col. 15, lines 44-49) including a library table that includes records of each library in the gene expression database including an identifier (LibraryID) (col. 16, lines 7-9). Lincoln et al. describe the library table as having a "TissueID" attribute that is inherited from a

"TissueSpecimen" table) and a "Tissue_Category" attribute as well as a "Lib_Description" attribute including information such as tissue name, disease state, patient age/gender (col. 16, lines 6-32). Lincoln et al. describe providing further information about a donor in a "MedicalHistory" table including information such as a problem such as breast cancer, breast, and neoplasm (col. 20, lines 33-40), as stated in instant claim 6. Lincoln et al. describe using a network to which the network server and clients are connected (col. 13, lines 3-9). Lincoln et al. describe entries in various results screens may provide links to other information in the database (col. 23, lines 10-13) as stated in instant claim 2. Lincoln et al. describe each tissue specimen (as uniquely identified by TissueID) may have several diagnoses (i.e. normal, diseased, involved, cancerous) and each donor may provide multiple tissue specimens (col. 19, lines 35-67). This act of providing multiple tissue specimens that are "cancerous" or "involved" is reasonably interpreted to include specimens from sites of a secondary metastasis of cancer, as stated in instant claim 16. Lincoln et al. describe different development stages (col. 20, lines 13-14) as stated in claim 11. Lincoln et al. describe studying or monitoring drug resistance in certain tissue (col. 5, lines 1-3) which represents substantially homogeneous cells (as stated in instant claim 13) and samples from patients treated with a drug (as stated in instant claim 15). However, Lincoln et al. do not describe using frozen cells or tissue, bodily fluid, 10% samples from different tissues, five different tumor types, samples greater than about 0.6 mm in diameter, and cancer-specific markers.

Schraml et al. describe using tissue microarrays for gene amplification surveys in many different tissue types (title). Schraml et al. describe using a tissue microarray consisting of samples from 17 different tumor types with 397 individual tumors arrayed in a single paraffin

block (representing at least about 10% of the samples of the microarray, as stated in instant claim 7) using minute tissue samples (diameter, 0.6mm) (abstract and Figure 1) which is greater than about 0.6 mm in diameter, as stated in instant claims 7, 8, and 9. Schraml et al. describe finding gene markers (i.e. CCND1) amplified in breast and other cancerous tissue types (abstract and page 1966, col. 2, first paragraph), as stated in instant claims 6 and 14. Schraml et al. describe hundreds of samples are precisely arrayed in a new paraffin block (page 1966, col. 2, second paragraph) which represents stably associated samples with distinct, known sublocations on a substrate, as stated in instant claims 1 and 4. Schraml et al. describe the precise positioning of tissue specimens to enable the generation of multiple replicate array blocks, each having samples from the same tissue specimens at identical coordinates (page 1970, col. 2), as stated in instant claims 1 and 4. Schraml et al. describe using frozen tissue samples from primary tumors (abnormally proliferating cells) and normal tissues (normally proliferating cells) and embedding the specimens in paraffin (page 1966, col. 2, third paragraph), as stated in instant claims 3, 5, and 10. Schraml et al. describe using tumors in different stages and grades, including 96 breast tumors (page 1967, col. 1, second paragraph), as stated in instant claims 11 and 12.

Lehman et al. describe studying breast cancer patients for activity of exon and intron base changes in the p53 gene (abstract). Lehman et al. describe patient information, such as age (abstract). Lehman et al. describe gene studies in response to drug treatment (abstract). In Table 1, Lehman et al. describe various statistics of patients including the stage of breast cancer. Lehman et al. describe coding the samples from patients and entering the information into a database (page 1063, col. 1, first paragraph). Lehman et al. describe collecting blood (bodily fluid) from breast cancer patients for analyses (page 1063, col. 1, first paragraph), as stated in

instant claim 4. Lehman et al. describe using paraffin-embedded tumor specimens and samples from patients undergoing drug treatments (page 1068, col. 1, third paragraph), as stated in instant claims 10 and 15.

Lehman et al. state the identification of woman at risk for development of breast cancer will have important implications for the prevention of cancers, treatment strategies, and improved cure rates of these patients (page 1062, col. 2, third paragraph). Schraml et al. state their tissue microarray technology has the potential to greatly facilitate analysis of alterations in multiple tissue types (page 1966, col. 2, second paragraph). Schraml et al. state that tumor arrays are a powerful tool to rapidly screen different tumor types for gene copy number alterations (page 1966, col. 2, second paragraph). Schraml et al. state they have demonstrated the power of using minute arrayed tissue specimens for tumor screening (abstract). Lincoln et al. state bioinformatics includes methods to search databases quickly to analyze information and make predictions (col. 1, lines 31-37). Lincoln et al. state information manipulation has been made easier to perform and understand with the development of sophisticated computer database systems (col. 1, lines 62-64). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make improvements to existing gene expression techniques tied to relational database systems, as stated by Lincoln et al, because even though these systems provide great power and flexibility in analyzing gene expression information, this technology is still in its infancy and further improvements are required to accelerate biological research for numerous applications (Lincoln et al. col. 2, lines 6-12). Therefore, it would have been obvious to one of ordinary skill in the art to improve efficiency of microarray analyses with minute frozen and bodily fluid samples from multiple cancer patients and multiple tumor types (as stated

by Schraml et al. and Lehman et al.) and relaying such information of relational database systems (as stated by Lincoln et al.) in order to accelerate research and evaluation in therapeutic pharmaceutical development and other fields by providing broad amounts of important information to clients in an easy to perform and understand format, as stated by Lincoln et al. (col. 1, line 62 to col. 2, line 28).

Thus, Lincoln et al., in view of Schraml et al. and Lehman et al., motivate the instant claims.

Applicants state that Lehman et al. and Schraml et al. recitations of a microarray do not anticipate an oncology microarray wherein each sample exhibits a biological characteristic representative of a stage of cancer. This is found unpersuasive as such a microarray with *each* sample exhibiting a biological characteristic representative of a stage of cancer appears to be NEW MATTER and not specifically mentioned in the instant application.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

July 19, 2004

Ardin H. Marschel 7/22/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER